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Review

The story behind the first few cases of monkeypox infection in non-endemic countries, 2022

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ABSTRACT

Starting May 6, 2022, a rising number of monkeypox cases started to be detected in different countries where the disease is not endemic. About 24 countries reported cases by May 28 mostly in Europe. Most of the reported cases so far were among young men particularly men who have sex with men or had a travel history to countries where cases are being registered. In this rapid review we summarized the story behind the first few cases of monkeypox virus infection in non-endemic countries and the prevention measures implemented so far by countries to contain the spread of the disease.

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Introduction

Monkeypox is a viral infection and a form of zoonosis (an infection transmitted to humans from animals) that is caused by

monkeypox virus [1]. The first human monkeypox was identified in 1970 in the Democratic Republic of the Congo and since then cases have been increasingly reported across regions in central and west Africa where it became endemic in such areas [2]. The first monkeypox outbreak outside Africa was recorded in 2003 in the United States of America (The 2003 Midwest monkeypox outbreak) [2]. During this outbreak, the first community-acquired human cases of monkeypox resulted from contact with infected prairie dogs that had been housed or transported with African rodents imported from Ghana [3]. This outbreak brought the disease to become of global

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public health importance since it was no longer limited in central and west Africa. At a time when the world was just about to start recovering from the negative repercussions of the COVID-19 pandemic, several countries started to report new cases of monkeypox infection. Taking the lessons learned from COVID-19 into account, many countries around the world even those who did not report any cases started to apply several preventive public health measures early, to contain the spread of the monkeypox infection. Epidemiological investigations particularly for the first few cases of an emerging infection such as monkeypox are critical to expand our knowledge about this disease which will inform the development of targeted public health guidance and policy decisions. People around the world need to have accurate, transparent information about the local and global situation of such escalating infection, and the way it spreads. Understanding the first few cases of this outbreak will facilitate timely estimation of the transmission patterns, and severity. For this, in this review, we will summarize the story behind the first few cases of the monkeypox 2022 outbreak, and the preventive measures imposed by countries to prevent and mitigate the infection.

Epidemiological and clinical characteristics of monkeypox

The monkeypox virus is an enveloped double stranded DNA virus that can infect various animal species mainly rodents [2,4]. Zoonotic transmission of the virus occurs by direct contact with blood, bodily fluids, or cutaneous or mucosal lesions of infected animals while human to human transmission can result from direct contact with respiratory secretions, skin lesions of an infected person or by indirect contact with recently contaminated objects such as bedding, clothing [2,5]. The human-to-human transmission via respiratory droplets requires prolonged face to face contact as the droplets can't travel more than few feet [5]. Clinical symptoms include rash, fever, chills, and lymphadenopathy which happens usually early in the course of illness and considered as a distinguishing sign that differentiate monkeypox from smallpox [6]. The incubation period of the virus ranges from 5 to 21 days but usually from 6 to 13 days [7]. Monkeypox is usually a self-limiting infection in most of the cases, yet it can be severe in certain population subgroups such as children, pregnant, and immunosuppressed individuals [8]. Two distinct genetic clades of the virus have been identified which are geographically separated and have defined epidemiological and clinical differences: the West African clade with case fatality rate of < 1 % and limited transmissibility, and the more severe clade known as Congo Basin clade (the Central African clade) with case fatality rate of nearly 11 % [9].

The first few cases of monkeypox infection reported in 2022 in non-endemic countries

Currently, the world is witnessing an ongoing outbreak of monkeypox infection as the first case was confirmed on May 6th in the **United Kingdom** in a British national who came recently from Nigeria where the disease is endemic and presented with signs and symptoms suggesting the disease [10]. The case was immediately hospitalized, isolated, and contact tracing started to identify all possible exposed contacts in the community, the international flight that brought him, and in healthcare setting where he sought medical attention. All possible contacts were being followed for 21 days for symptoms development [10]. Later, the contact tracing extended to Scotland after identifying a small number of people as being close contacts of the case identified in England [11].

On May 12, another two cases who live in the same household were identified in the United Kingdom (in London) who had no links with the first case and no history of traveling to endemic

countries [12]. One of these cases was hospitalized and the other self-isolated at home.

On May 17 the United Kingdom Health Security Agency (UKHSA) confirmed four more cases (three in London, and one in north-east England with a travel history to London) [13]. The cases had no links with the previous three cases confirmed earlier and the country started to investigate any potential links between the new four cases. All the four self-identified themselves as gays or bisexual [13].

On May 18, **Portugal** health officials confirmed the first five cases of monkeypox among men between 20 and 50 years who were identified in the setting of sexually transmitted diseases clinic due to genital lesions [14]. All of them were men who have sex with men [14]. On the same day, the **Spain** Health Ministry confirmed the first seven cases in Madrid along with another 22 suspected cases [15]. All of them were men and two out of the seven cases were hospitalized [15]. Most of the cases confirmed were linked to a sauna known to be a “gay friendly” establishment [16]. The first case in the **United States of America** was detected in Massachusetts in a man with recent travel history to Canada [17]. The man was hospitalized on May 12 and was diagnosed 6 days later [18].

On May 19, **Sweden** has announced the first confirmed case of monkeypox, followed by the second case confirmed on May 26 [19]. The country did not announce the results of the case investigations; however, it considered the infection as a public health risk [20]. Similarly, the first case was confirmed in **Italy** in a symptomatic man who had a recent travel history to the Canary Islands. Two more cases that were linked to the first case were confirmed on May 20, and all the three were hospitalized [21]. Another two cases were confirmed in **Belgium** on May 19 and May 20 from different cities [22]. The first three cases detected in Belgium were linked to a large-scale festival in the port city of Antwerp [23]. Similarly, the first two cases in **Canada** were confirmed on May 19 among men in the Province of Quebec [24].

On May 20, **Australia** recorded the first two cases of the infection. The first one in Melbourne for a man in his 30s who developed mild symptoms after returning to Melbourne from the United Kingdom [25]. The department of health in Victoria started the contact tracing which included the passengers seated near him in the flights from London to Abu Dhabi, and from Abu Dhabi to Melbourne and asked close contacts to self-isolate only if developed symptoms [25]. The second case was a man in his 40s with mild symptoms who returned to Sydney from Europe [26]. Also, **France's** Ministry of health announced the first case on May 20, in a 29-year-old man who denied any recent travel history to a country where the disease is being reported [27]. Moreover, **Germany** confirmed its first case in a 26-year-old man in the southern city of Munich, who had traveled from Portugal via Spain [28]. **Netherlands** registered the first case of monkeypox on May 20 in a man but few days later the number of cases rose to six and all cases were men who have sex with men and some of them attended the Darkland festival in Belgium [29].

On May 21, **Switzerland** and **Israel** announced their first cases. The one in Switzerland in the canton of Bern is a man who contracted the virus through “close physical contact abroad”. While the one in Israel is a 30-year-old man, who recently returned from western Europe with monkeypox symptoms. On May 22, **Austria's** first case was registered in a 35-year-old man who presented with fever and rash in Vienna [30]. On May 23, **Denmark** confirmed the first case in an adult male who had recently returned from Spain [31].

On May 24, **The Czech Republic** registered the first case in a female who recently attended a festival in Belgium [32], and **The United Arab Emirates (UAE)** has become the first gulf state to register a monkeypox case in a 29-year-old female visitor who came from West Africa [33]. Similarly, **Slovenia** reported the first case in a

Table 1
Summary of the first few cases of monkeypox detected in non-endemic countries in 2022, as of May 28, 2022.

Country	Date of first case	Sex	Possible Links	Total number of cases*
United Kingdom (UK)	May 6	Male	Travel history to Nigeria	106
Portugal	May 18	Male	MSM	74
Spain	May 18	Male	Sauna that is gay friendly	106
United States of America	May 18	Male	Travel history to Canada	9
Sweden	May 19	NA	NA	2
Italy	May 19	Male	Travel history to Canary Islands	12
Belgium	May 19	NA	Attended a festival in Belgium	7
Canada	May 19	Male	NA	26
Australia	May 20	Male	Travel History to UK	2
France	May 20	Male	NA	7
Germany	May 20	Male	Travel history to Portugal and Spain	21
Netherlands	May 20	Male	MSM, travel history to Belgium where he attended a festival	12
Switzerland	May 21	Male	Travel history and close physical contact	4
Israel	May 21	Male	Travel history to western Europe	2
Austria	May 22	Male	NA	1
Denmark	May 23	Male	Travel history to Spain	2
The Czech Republic	May 24	Female	Travel history to Belgium where she attended a festival	5
The United Arab Emirates (UAE)	May 24	Female	Travel history to West Africa	1
Slovenia	May 24	Male	Travel history to Canary Islands	2
Argentina	May 27	Male	Travel history to Spain	2
Finland	May 27	Male	Travel history to Europe	1
Ireland	May 28	NA	NA	1
Malta	May 28	Male	Travel history (country not disclosed)	1
Mexico	May 28	Male	Travel history to Netherlands	1
Total Number				407

Abbreviations: MSM, men who have sex with men; NA, not available.

* Source: <https://monkeypox.healthmap.org/>.

man who recently returned from the Canary Islands and developed symptoms upon arrival to Slovenia [34]. The first monkeypox case in the South American nation was registered in **Argentina** on May 27, in a 40-year-old man who developed symptoms including fever and blisters after recently returning from Spain [35]. **Finland** also registered its first case in a male who recently returned from a trip to Europe. Close contacts with the infected person have been traced and instructed to self-isolate to prevent any possible spread of the virus [36]. On May 28, the first cases were registered in **Ireland, and Mexico**. Ireland did not disclose any information about the case [37]. The case in Mexico was a 50-year-old man who recently returned from Netherlands [38].

By May 28, the total number of cases detected in non-endemic countries exceeded 400 [39]. By the time of writing this review, no deaths have been recorded among infected cases, and most of the cases were mild. Table 1 summarizes what is already known about the first few cases of monkeypox 2022 in non-endemic countries.

Preventive measures imposed by countries to contain the spread of monkeypox

As the monkeypox virus is making headway across Europe and other non-endemic countries, more cases are expected to be registered and countries worldwide—even those with no reported cases yet—need to start implementing the necessary public health measures to prevent and contain the spread of the infection. Countries with reported cases started the contact tracing and have been following the contacts for symptoms development. Belgium was the first country to introduce a compulsory 21-day quarantine for infected patients while contacts need not to self-isolate but must stay vigilant and watch for any symptom development [40]. On the other hand, UK is advising those with direct or household contacts to self-isolate for 21 days [41].

Following the confirmation of the first monkeypox case in the United States, the government ordered what equals a \$119 million US dollars of smallpox Vaccines which are also effective against monkeypox from Bavarian Nordic company [42]. The vaccine known as JYNNEOS (marketed under the brand names IMVANEX and

IMVAMUNE in the European Union and Canada) is based on a live, attenuated vaccinia virus which is cultured in chicken embryo fibroblast cells and was Approved by the U.S. Food and Drug Administration (FDA) in 2019, and by the European Medicines Agency in 2013 for preventing smallpox and monkeypox disease in adults 18 years of age and older who are at high risk for smallpox or monkeypox infection [43]. The vaccine has 85 % effectiveness against monkeypox virus [2]. The UK started to give IMVANEX as a post exposure prophylaxis for close contacts of confirmed cases [44]. For post exposure prophylaxis, the vaccine should be administered in the first four days of exposure. Giving it 4–14 days post exposure can reduce the symptoms but does not prevent the infection [45]. Many countries started to prepare their emergency preparedness plans to deal with monkeypox. The UAE prepared a comprehensive guide for surveillance, early detection of the disease, management of clinically infected patients, and other precautionary measures. The Ministry of health and prevention also issued a circular for all medical cadres working in the country requesting them to report any suspected case to competent health authorities [46]. Similarly, the Ministry of public health in Qatar asked the public and the private sectors to monitor for potential patients presenting with symptoms suggesting monkeypox and to report any suspected cases to the health authorities [47]. It also issued a pathway illustrating the way of dealing with suspected cases presenting to health facilities.

The World Health Organization (WHO) has warned that stigmatizing people with the infection can hinder the outbreak mitigating efforts and may prevent people with symptoms to seek medical care leading eventually to undetected spread [48]. As of May 29, no travel bans, or restrictions have been imposed by countries to halt the spread of the infection.

Discussion

This review showed that the first monkeypox cases were mainly detected among men. Based on currently available information, many of the cases recorded worldwide so far are among men who have sex with men (MSM) who presented to sexually transmitted diseases clinics due to development of symptoms including rash at

the genital areas [7]. The disease is not known to be sexually transmitted but the close direct contact with lesions can transmit the virus and explains why many of the cases occur among MSM [49]. This should alert countries to provide the necessary public health advice on the mode of transmission of the disease and the necessary precautions, and work closely with healthcare providers in different settings mainly in sexually transmitted disease clinics and primary care settings to report any suspected cases based on the definitions provided by the WHO.

Most of the cases discussed in this review had a recent travel history to a nonendemic country where cases were recorded as shown in Table 1. It is of high importance to assess travel history of those presenting with monkeypox symptoms and to advise those with recent travel history who develop symptoms to seek medical attention immediately. No travel bans were imposed until the moment of writing this review, but the upcoming weeks and the progress of the outbreak might prompt some travel restrictions if the transmission accelerated.

Several cases had history of attending large scale festivals as described above and this can be concerning especially with more festivals, parties and gatherings are expected during the summertime. Such gatherings usually entail prolonged close contact and interaction among attendees which might put them at risk of exposure to the virus. Countries need to educate the public about the risk of transmission in such environments and how to protect themselves against catching the infection. Almost all the countries with confirmed cases announced that they started the contact tracing process. Starting the contact tracing early can interrupt the disease transmission and help those at high risk for severe disease to be identified and receive the needed medical care more quickly and promptly [7]. It is highly unusual that cases are detected without travel links to endemic areas which might necessitate expanding the surveillance process.

This review was limited by the scarcity of information available about the first few cases of monkeypox 2022 outbreak. Many countries did not disclose the age of the confirmed cases.

Conclusion

The number of monkeypox confirmed cases is increasing daily, and more cases are expected to come. Most of the cases have been detected among men, several identified themselves as gays or bisexual. Most cases sought medical attention due to the development of symptoms mainly rash. This is the first-time, chains of transmission are reported in Europe without known epidemiological links to West or Central Africa where this disease is endemic. Countries need to take the lessons learned from COVID-19 pandemic to act early and promptly to prevent or contain the spread of the disease.

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Code availability

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Muna Abed Alah: conceptualized the idea, wrote the paper, Sami Abdeen, and Elias Tayar: wrote the paper, lheb Bougmiza: provided final review.

Consent

not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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